Medical Cannabis 2022

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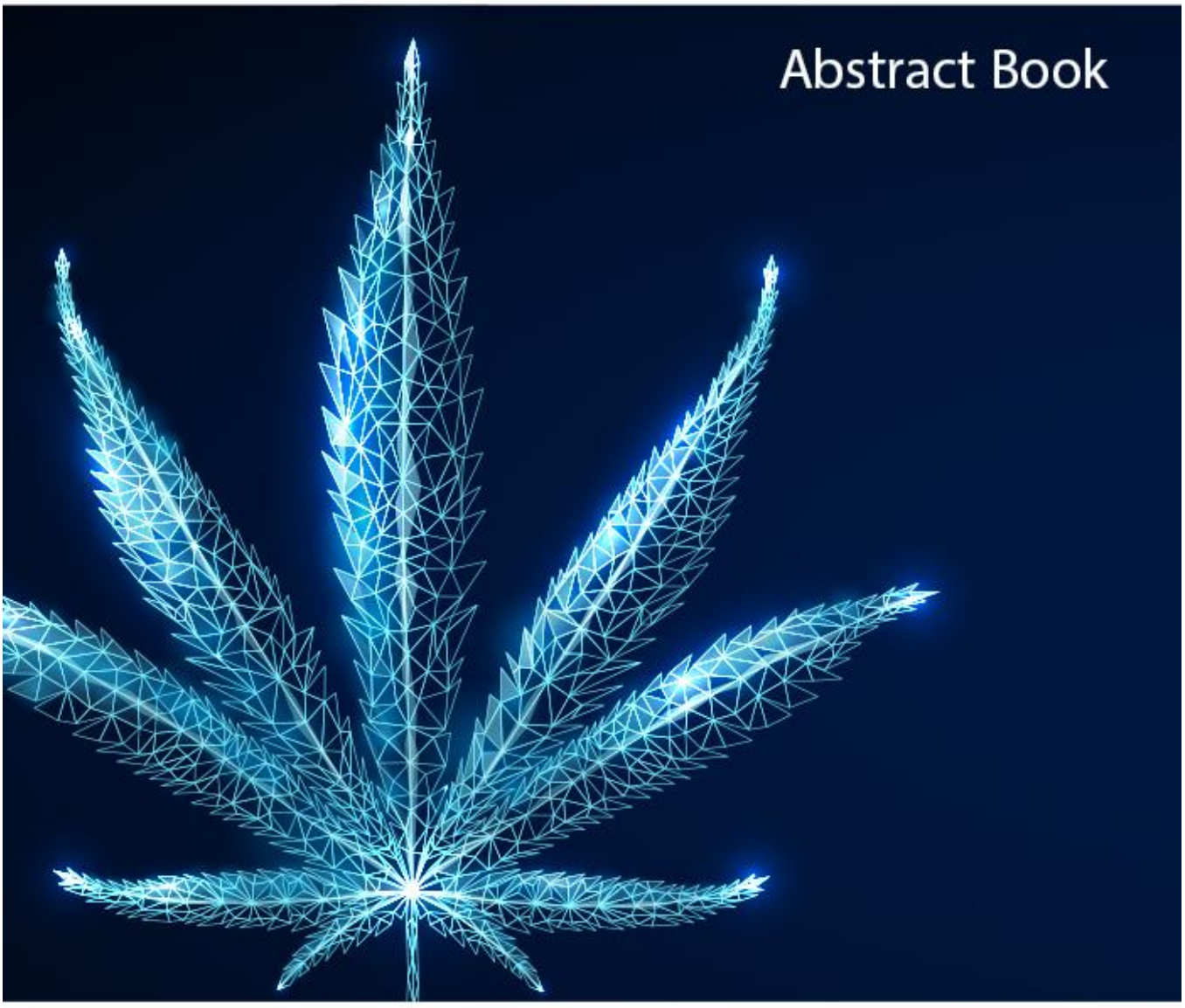

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Poster 60

Clinical Studies

Economic Evaluations of Cannabinoids in the Symptomatic Treatment of Multiple Sclerosis: a Scoping Review

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Background: Nabiximols contains tetrahydrocannabinol and cannabidiol and is the only cannabinoid-based medicine with an indication for spasticity in multiple sclerosis (MS). The evidence regarding the economic impact of the symptomatic treatment of MS with cannabinoids is mixed and is mainly focused on spasticity.

Objective: To update the evidence from economic evaluations of cannabinoids in alleviating any MS symptom, considering the legalization of their medical or recreational use.

Methods: We conducted a literature search on August 21-22, 2022, using keywords for MS, cannabinoids, and economic evaluations. No language or date restrictions were applied. Databases: MEDLINE, Embase, CINAHL Complete, PsycINFO, EconLit, ProQuest Dissertations & Theses Global, Web of Science, Cost-Effectiveness Analysis Registry, National Health Service Economic Evaluation Database, Health Technology Assessments (HTA), the international HTA database, and websites of HTA agencies.

Results: From 1164 references, 19 were included to illustrate the available evidence, from which 17 were considered for data extraction and the remaining two were systematic reviews. Most of them were cost-utility analyses, assessing nabiximols for spasticity. Canada, the United Kingdom, Italy, Belgium, Switzerland, Sweden, Spain, Germany, and Brazil were the retrieved settings. None had legalized the recreational use of cannabis at the time of their respective studies.

Conclusion: Seven studies considered nabiximols to be cost-effective or dominant, one reported a positive willingness to pay outcome, and three concluded that cannabinoids are not cost-effective. The remaining studies had unclear conclusions. There is an evidence gap for other cannabinoids, other symptoms of MS, and the economic impact of legalizing these products.

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Clinical Studies

Should Mothers who Use Cannabis Absolutely Abstain from Breastfeeding?

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Background: between 1 and 6 months of age, the infant is breastfed on average 100 mL (+/- 15 mL), 11 times (+/- 3) per day. In a recent study, for mothers consuming cannabis at 23.18% THC, the average absolute infant dose of THC was estimated at 8 µg/kg/day [Baker T. et al. Obstet Gynecol. 2018; 131: 783-8]. Studies state marijuana exposure via the mother's milk during the first month postpartum appears to be associated with a decrease in infant motor development at 1 year of age. With legalization of marijuana and the therapeutic cannabis, some publications recommend not breastfeeding for mothers who use cannabis.

Objective: to investigate the nursing mother's consumption of cannabis by searching for the presence of cannabinoids in breast milk and, in case of positivity, to assess the ratio benefit/risk of breastfeeding.

Methods: using GC-MS, we measured THC, OH-THC and THC-COOH (LOQ: 0.5, 0.5 and 2 ng/mL, respectively) in 4 nursing mothers' breast milk (day 2, day 4, day 20 and day 26, respectively), smoking one to three joints/day (no THC standardization) and measured THC-COOH in their children's urine. Favorable opinions were obtained from the 2014 and 2021 CHT Ethics Committees.

Results: concentrations in breast milk ranged from 1,16 to 16.20 ng/mL for THC; from not detected to 65.5 ng/mL for THC-COOH; OH-THC has never been detected. Infants' urine samples were all negative and clinical evaluations were normal.

Conclusion: studies should be carried out on a much larger scale; one of the difficulties is to be able to quantify the dose of THC consumed by mothers and the role of prenatal marijuana exposure. However, the importance of breastfeeding is no longer to be demonstrated, in particular regarding the immune protection of the newborn and the quality of maternal/infant interactions. We propose not to stop breastfeeding for cannabis users whose infant's urine remains negative using a sensitive screening method, especially since these children have already been exposed in utero to cannabis.

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Clinical Studies

Glioma: Reducing Anxiety by ConSuming CannabinoidS – The GRASS Study Protocol

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Background

Gliomas are primary brain tumors that are incurable to date. Due to a short life expectancy, maintaining or improving quality of life is essential in these patients. The main symptoms that affect quality of life in glioma patients include anxiety and depressive mood. Approximately a third of glioma patients currently use non-medicinal cannabinoids for presumed symptom relief. Systematic studies that investigate the effect of cannabinoids on well-being are lacking in this population.

Objectives

To investigate the effect of a three-week treatment with cannabidiol (CBD) on anxiety levels in stable glioma patients.

Methods

In this double-blind, placebo-controlled crossover study, 55 glioma patients will be included. Only patients with stable disease will be included, so without clinical or radiological progression during the previous two months. Patients will be randomized to CBD or placebo as first treatment, which will be administered during three weeks followed by a washout period of 2.5 weeks before the second treatment period starts. All patients will alternately receive both 600 mg CBD and a placebo. The primary endpoint is anxiety as measured by the difference in the State subscale of the State-Trait Anxiety Inventory (S-STAI) after three weeks of treatment compared with baseline. Secondary objectives include depression, fatigue and quality of life. Liver functions will be monitored every three weeks and patient-reported adverse events weekly.

Conclusion

This randomized-controlled, crossover trial will investigate the effects of CBD on anxiety in stable glioma patients. Recruitment has started in February, 2022.

Trial Registry

https://trialsearch.who.int/Trial2.aspx?TrialID=EUCTR2020-004294-48-NL

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Basic Science

Is Antioxidant Activity Responsible for the Pleiotropic Effects of Cannabis sativa?

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Background

Oxidative stress is associated among others with cardiovascular disease, neurodegenerative diseases, cancer and diabetes. The destructive action of free radicals affects healthy cells impairing them and leading to a chain reaction of further damage. In diabetes, as an example, oxidative stress intensifies, damaging pancreatic cells and leading to nephropathy and microangiopathy. Formulations containing extracts from Cannabis sativa are likely to be used in treating pain, inflammation, autoimmune diseases, and even cancer but also appear to reduce the risk of chronic diseases such as diabetes and neurodegenerative diseases. The mechanism of action of cannabis is probably based on its effect on the endocannabinoid system. However, the importance of oxidative stress in the development of diseases suggests that the antioxidant activity of hemp is crucial, providing a multidirectional effect. Due to the `entourage` effect of the compounds contained in the raw material, potent antioxidant activity is possible, providing protection of cells from damage and preventing the development of various diseases.

Objectives

The study aimed to evaluate the antioxidant activity of three hemp cultivars - Bilobrzeskie, Tiger, and Henola - and relate it to the content of active compounds.

Methods

In vitro methods using the scavenging capacity of 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2′-azinobis-3-ethyl-benzothiazoline-6-sulfonate (ABTS), and ferric reducing antioxidant power (FRAP) were applied.

Results

Each extract showed strong antioxidant properties. The antioxidant activity depended on the CBD, CBG, and THC content, the extraction method, and the solvent used.

Conclusion

Cannabis sativa shows strong antioxidant potential, preventing the effects of oxidative stress, which may correspond to their pleiotropic health-promoting effects.

This study was funded by a grant from the National Science Center, PRELUDIUM BIS, 2020/39/O/NZ7/03441

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Clinical Studies

Safety and Tolerability of Oral Cannabinoids in People Living with HIV on Long-Term ART: a Randomized Pilot Clinical Study

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Background: Cannabinoids may reduce persistent detrimental immune activation in people living with HIV (PLWH) receiving antiretroviral therapy (ART). Their safety and tolerability are not well established.

Methods: We conducted an open-label interventional pilot study at the McGill University Health Centre in Montreal, Canada. PLWH virologically suppressed on ART were randomized to oral Δ9-tetrahydrocannabinol (THC): cannabidiol (CBD) combination capsules (THC 2.5 mg/CBD 2.5 m) or CBD-only capsules (CBD 200 mg). Individuals titrated their dose as tolerated to a maximum daily dose THC 15/CBD 15 mg or 800 mg CBD, respectively, for 12 weeks. The primary outcome was the percentage of participants without any significant toxicity determined using the WHO toxicity scale (Grades 0-2 scores).

Results: Ten individuals (median age 58 years[IQR 55, 62]) were randomized, 5 in each group. Eight completed the study without signs of toxicity. Two were withdrawn at 6 weeks while taking 800 mg CBD daily, due to safety concerns. One discontinued the study due to study procedures (phlebotomy aggravating pre-existing anemia) and one due to severe hepatitis at the 800 mg CBD dose in the context of newly discovered pancreatic adenocarcinoma. Cannabinoids did not alter hematology or biochemistry profiles. CD4 count, CD4/CD8 ratio, and HIV viral suppression remained stable. Most adverse effects were mild to moderate, with somnolence being most common, and managed by dose reduction.

Conclusion: In PLWH, cannabinoids seem generally safe and well-tolerated, though larger studies are needed. However, careful screening for occult liver pathology should be performed and hepatic enzymes monitored during therapy, especially with high CBD doses.

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Basic Science

Molecular Modeling Targeting the ACE2 Receptor with Cannabis sativa's Active Ingredients for Antiviral Drug Discovery Against SARS-CoV-2 Infections

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Background

The emergence of novel coronavirus caused desperation within the communities and increased interest in exploring medicinal plant-based therapeutics to treat and prevent SARS-CoV-2 virus infections, as many medicinal plants have been reported to have antiviral, anti-inflammatory, and immunomodulatory effects.

Objectives

This exploratory study seeks to dock the bioactive components of Cannabis sativa, a natural plant with several pharmacological and biological properties, with the ACE2 receptor.

Methods

The protein and ligand structures were optimized using AutoDock Tools. Molecular docking experiments were performed using PyRx software. The best pose of the compounds predicted was observed using PyMOL and DSV tools. The SwissADME server predicted molar refractivity, saturation, and promiscuity. pkCSM was used to screen for chemical ADMET attributes.

Results

Three Cannabis sativa active components have been found to bind to the ACE2 protein active site and could inhibit spike binding. 6-Prenylapigenin, cannabivarin (CBN-C3), and Δ8-tetrahydrocannabinolic acid-A (Δ8 –THCA) have a greater affinity (-8,3 kcal/mol, -8,3 kcal/mol, and -8,0 kcal/mol, respectively) and satisfactory interaction with ACE2 than its inhibitor MLN-4760 (-7,1 kcal/mol). These potential drugs have good ADMET values.

Conclusion

Inhibiting the interaction between the viral Receptor Binding Domaine and host ACE2 presents a promising strategy for blocking SAR-COV-2 entry into human cells and upregulating ACE2 expression. Our research reveals that 6-Prenylapigenin, cannabivarin (CBN-C3), and 8-tetrahydrocannabinolic acid-A (8-THCA) are tree compounds that have shown promising binding and drug-likeness outcomes, which should be evaluated further for pharmaceutical development research.

Keywords: Medicinal Plant, Cannabis sativa, COVID-19, SARS-CoV-2, ACE2, Spike, Drug discovery, Molecular docking, ADMET

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Basic Science

Cues of Anti-Inflammatory Activity Induced by Cannabidiol (CBD) on the Monocyte/Macrophage THP-1 Cell Line.

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Abstract

Introduction: Cannabidiol (CBD) is the main non-psycho-active component of the Cannabis sativa. Like other psycho-active cannabinoids (i.e. THC), CBD is an immune-modulating agent that affects T cells, B cells, macrophages and microglia cells. Several studies have shown the cannabinoids' ability to suppress inflammatory response, reducing pro-inflammatory cytokine expression and increasing levels of anti-inflammatory cytokine.

Objective: Aim of this study was to investigate mechanisms related to the immunomodulation triggered by cannabinoids, with focus on the CBD anti-inflammatory ability. The investigation was conducted on immunocompetent cells using the THP-1, an established leukemic monocytic lineage, able to differentiate into macrophages upon PMA treatment.

Methods: THP-1 cells pre-activated with PMA (1 µg/mL) for 3 days according to the procedures, were pre-incubated with CBD 0.3 and 1 µM for 1h, and subsequently, cells were treated with LPS (5µg/mL) for 24 and 48h, respectively, in order to stimulate inflammatory response. Supernatants were then analysed using the ELISA assay.

Results: As expected LPS treated macrophages increased their pro-inflammatory IL-6 expression. Pre-treating cells with CBD reduce the IL-6 expression and increase IL-10 expression. These variations in inflammatory interleukins levels are more significantly after 48 hours and for cells treated with the higher concentration (1 uM) of CBD.

Conclusions: The cells treated with CBD showed a reduced expression of pro-inflammatory IL-6 and an increasing of anti-inflammatory IL-10. These findings confirmed CBD anti-inflammatory ability, suggesting that it may have therapeutic potential for inflammatory diseases.

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Clinical Studies

NSW Cannabis Medicines Advisory Service Retrospective Database: Preliminary Data Analysis (2021 to mid-2022)

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Background

Following regulatory changes providing increased access to cannabis medicine in Australia, an innovative New South Wales (NSW) government-funded state-wide medical advisory service on cannabis medicines operated between 2018 and mid-2022. The service model, led by a clinical pharmacologist and pharmacists, provided comprehensive patient-specific and evidence-based information to support health professionals in prescribing and patient-care decisions.

Objective

Describe real-world data collected as part of the day-to-day operation of a medical advisory service for cannabis medicines.

Methods

A retrospective analysis of data collected between January 2021 and June 2022 was conducted using descriptive statistics. The variables of diagnosis, indication and comorbidities were double MedDRA coded and a coding consensus was reached.

Results

A subset of enquiries containing detailed patient-specific information was analysed (n = 124/567; 21.9%). The majority of enquiries were from general practitioners (n = 102/124; 82.3%).

Female (n = 53/124; 42.7%) and male (n = 59/124; 47.6%) patients were similarly represented and were mainly 31-50 years of age (36/124; 29.0%). The top three diagnoses were osteoarthritis, anxiety and chronic pain. Top indications for use were chronic pain, anxiety, non-neuropathic pain, insomnia and back pain. Comorbidities mainly included hypertension, depression and hypercholesterolaemia. Comedications were most commonly non-opioid and opioid analgesics and antidepressants.

The service was contacted by medical and allied health professionals regarding management of potential adverse events for five patients, including renal and urinary, vascular, nervous system and psychiatric disorders.

Conclusion

Service data highlights key areas, including but not limited to polypharmacy and complex patient comorbidities, where health professionals can be supported with evidence-based information to inform patient care decision-making.

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Clinical Studies

Cannabis Oil Treatment for Sedative-Resistant Agitation in the Intensive Care Unit

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Background: In ICU patients agitation is a common phenomenon. Underlying causes are known to be, but not limited to, pain, delirium and drug- or alcohol withdrawal. Not only is treatment of agitation important to improve patient comfort; agitated patients may impose safety hazards onto themselves, as agitation is associated with self-detubation and worse clinical outcomes.

Case: We present a patient with a history of cannabis- and alcohol abuse in which high doses of multiple conventional sedative agents were insufficient to relieve agitation. The associated motor restlessness and tachypnea hindered Spontaneous Breathing Trials while intubated, and prohibited weaning from mechanical ventilation after tracheostomy was performed. In an effort to relieve the agitation, drops of cannabis oil were administered to the patient`s oral mucosa. Within hours of first administration, almost all conventional sedatives could be ceased. Symptoms of agitation were relieved, the patient remained calm, cooperative, and his quality of sleep improved during the whole further course.

Conclusion: We successfully treated agitation by administering cannabis oil to a mechanically ventilated patient in the ICU, with a history of recent cannabis abuse, who exhibited agitation that could not be adequately managed with conventional sedative agents. Our findings suggest that cannabis oil could be an effective alternative to the conventional pharmacological arsenal of sedatives in the Intensive Care Unit, in patients who are regular cannabis users.

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Clinical Studies

The Use of Cannabis in Anosmia and Ageusia in a Female with Brain Glioblastoma – a Case Report

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The medical cannabis act brought new opportunities in palliative care in Poland in 2017.
Herbal cannabis is registered in Poland as pharmaceutical raw material and not as medication. Therefore, it does not have the characteristics of the medicinal product or indications for use, allowing its wide use in the symptomatic treatment of cancer. In the described case of a 37-year-old female with anosmia, ageusia, and a loss of appetite in the course glioblastoma, which resulted in a lack of appetite, we used vaporized cannabis flos/lemon skunk Red No.2 containing THC 19% +/- 10% and CBD 1% administered 0.25 g q.i.d. The patient was dissatisfied with the previous treatment, which, according to her, did not bring the expected effect. Herbal cannabis improved the sense of smell, taste, and increased appetite, which effects maintained for 2 hours after vaporization.
The case study reports an improvement in the patient`s sense of taste and smell, which directly led to increased appetite and improved quality of life.

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Clinical Studies

Sex-Dependent Prescription Patterns and Clinical Outcomes Associated with the Use of Two Oral Cannabis Formulations in the Multimodal Management of Chronic Pain Patients in Colombia

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Background: This is the first study on the clinical use of cannabis-based magistral formulations (CBMF) in Colombia since its regulation in 2017.

Objectives: To characterize the prescription patterns and clinical outcomes associated with the use CBMFs in the multimodal management of chronic pain in Colombian adults.

Methods: An observational retrospective cohort study was conducted by revision of medical records of patients with chronic pain. Participants were asked to score their symptomatic improvement in an 11-point numeric analog scale (NAS) and to report any side effects associated to their treatment with CBMFs. Patient-reported outcome measures (PROMS) were analyzed by i) the sex of the patient; ii) prescribed CBMF; and iii) duration of treatment.

Results: 2112 patients participated in the study, a majority of which were female (76.1%) with an average age of 58.7, ranging from 18 to 98. Older adults (65) represented 46.4% of the cohort. A chemotype-II and a chemotype-III formulations accounted for 59.5% and 39.8% of all prescriptions, respectively. Prescription patterns showed significant sex bias (Z=6.807, p0.001). Most participants (92.7%) reported a reduction (5.5±2.5, p0.001) of their chronic pain symptoms associated to the treatment with CBMFs. Females showed a faster improvement and effects were sustained in the long term (+26 weeks). No adverse side effects were reported by most participants (71.7%) and those noticed were mild, such as somnolence (13%), dizziness (8,1%) and dry mouth (4,3%).

Conclusion: Evidence accrued through real-world clinical experience can help inform best medical practices to maximize therapeutical effectiveness and tolerability of medicinal cannabis.

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Basic Science

Effect of "Full Spectrum" and "Broad Spectrum" Cannabidiol (CBD) Oil In Comparison To Purified CBD on A Novel Human "Leaky Gut" Triple Cell Co-Culture Model

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The "leaky gut" syndrome describes a damaged (leaky) intestinal mucosa and is considered a serious contributor to numerous chronic diseases. This syndrome is especially associated with chronic inflammatory bowel diseases (Crohn`s disease, ulcerative colitis), but also allergies, asthma, and autoimmune diseases. We investigated here the effect of commercially available "full spectrum" and "broad spectrum" cannabidiol (CBD) oil products in comparison to pure CBD, using a novel human in vitro leaky gut model of the small intestine. This inverted triple-culture model consists of 21-day-differentiated human intestinal Caco-2 epithelial cells, and HT29-MTX-E12 mucus-producing goblet cells (ratio 90:10), cultured on the upper part of transwell-membrane inserts. On the bottom side of the insert, differentiated human monocytic THP-1 cells were co-cultured. For modeling a leaky gut condition, cells were triggered into an inflammatory state, which was determined by quantification of transepithelial electrical resistance (TEER), and cell passage of fluorescein isothiocyanate-dextran 4 kDa (FD4). Pro-inflammatory cytokines were assessed using ELISA. While no effect could be found on triggered cytokine release, apical application of CBD/CBD products promoted the recovery from intestinal integrity loss, but with different potency. Based on the results of our novel in vitro leaky gut model, other bioactive compounds besides CBD may also be important in modulating abnormal small intestinal permeability.

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Basic Science

Local Cannabidiol Application in Vulvovaginal Atrophy

Gudrun Lorenz-Eberhardt, **Gudrun Lorenz-Eberhardt**

Background: Vulvovaginal atrophy becomes apparent approximately 2-3 years after menopause and is a progressive process. In contrast to the vegetatively mediated menopausal symptoms, the urogenital symptoms do not decrease but lead to persistent, sometimes irreversible changes in the vagina and vulva. 45-63% of postmenopausal women suffer symptoms- dryness, itching, burning, irritable bladder, dyspareunia.

Objectives:

Many women are asking about non-hormonal alternatives to treat a relieve VVA symptoms. Can cannabidiol relieve symptoms locally and does the clinical picture improve?

Methods:

259 women aged 50-80 years, typical symptoms caused by VVA, gynecological examination: moderate to pronounced signs of atrophy. Daily application of a CBD-containing ointment to the vulva and once a week intravaginal application of a CBD- containing suppository.

Results:

All women reported a significant decrease in their symptoms. Objectively, the gynecological examination showed a significantly improved finding of vulva and vagina.

Conclusion:

The use of cannabidiol-containing ointments and vaginal suppositories leads to very good therapeutic success and subjective freedom from symptoms when used regularly.

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Basic Science

Finding Accurate THC Level in CBD

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In South Korea, tetrahydrocannabinol (THC) is an illegal substance, thus THC level is the key issue of medical Cannabis in South Korea.

THC is also contained in many foods which is legally distributed, so we tried to find references for appropriate level of THC by detecting THC level in foods.
So we tried to compare THC level in seed oil which is legal food in South Korea, to THC level in CBD

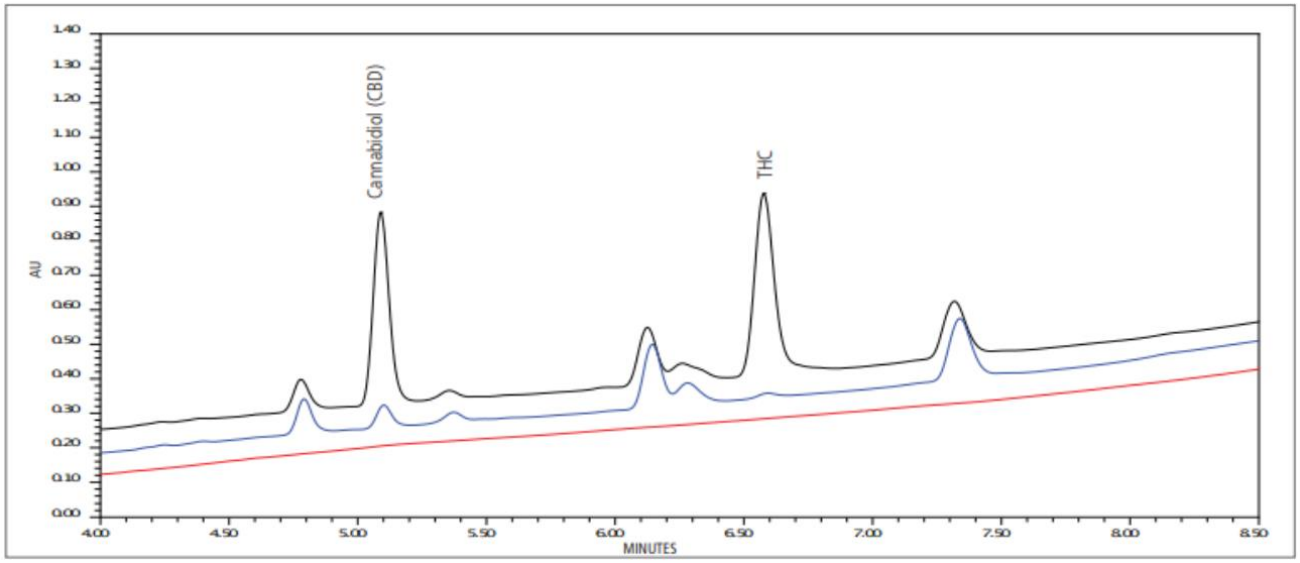
Method
The level of THC is vularnable in room temperature and is hard to detect.
Therefore, we recommend and suggest the method to qualify the THC level in CBD by using specified HPLC system (below).

Korea.

PerkinElmer Altus™HPLC system
A-10 Solvent/Sample Module
A-10 column heater
A-10 UV detector
A-10 PDA detector
Column : PerkinElmer Brownlee™SPP C18, 2.7 µm, 3.0 x 100-mm
Solvent and diluent : HPLC-grade
Filter : via 0.45-µm
Hardware/Software

Results

Using this specified HPLC system, we compared THC level in hemp oil and CBD



Hemp Seed Oil	CBD (%)	THC (%)
Brand A spiked	91.0	96.6
Brand B spiked	95.6	110.2

Overlaid chromatograms of a blank (red), Brand 2 un spiked hemp seed oil (black) and Brand2 hemp seed oil spiked with 125 ppm THC and CBD (blue).Recovery results for hemp seed oil spiked with THC and CBD at 125 ppm (n=2)

THC was also detected in seed oil and peak level was 0.4 ppm. We think if THC level is lower than 04 ppm in CBD, it will be no risk for drug addiction.

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Clinical Studies

Can Cannabidiol (CBD) Reduce Anxiety and Depression? PROMIS-29 Questionnaire Results from a Patient Registry.

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Over the past twenty years, research into the non-psychoactive cannabis compound cannabidiol (CBD) has increased significantly, with eight PubMed-listed publications per year in 2001 to 1000 in 2021. CBD is FDA approved for rare genetic childhood epilepsy. Additionally, many patients self-medicate with CBD for chronic pain and mental health conditions. Our patient registry was designed to learn more about participants` self-medication and potential improvements of their conditions.

A Patient Registry was designed in which access to a well-controlled and tested CBD formulation was provided. It included a survey asking the PROMIS-29 health questionnaire and experience surrounding CBD products. Exempt status was granted after IRB review, and we utilized the internet survey platform SurveyMonkey to administer the survey online.

Of our participants, 177 completed the baseline and one-month survey. We found a significant decrease in several PROMIS-29 domains. Anxiety changed from the ‘moderate’ to ‘mild’ category, and the T-score decreased by 3.7 points. Depression changed from ‘mild’ to ‘normal’ with a decrease of 3.9 points. Other domains such as ‘fatigue,’ ‘sleep disturbance,’ ‘pain interference,’ and ‘pain intensity’ showed statistically significant results while their category did not change.

The data show a reduction of T-scores across multiple domains with clinically significant decreases in anxiety and depression after one month of access to a well-controlled CBD formulation. As a study limitation, the voluntary nature of a survey-based design needs to be mentioned. However, survey studies can help generate hypotheses and identify areas of interest that future research can aim to answer.

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Clinical Studies

Adjuvant Treatment with Cannabinoids in Non-Cancer Pain in Patients Treated in Pain Clinics in Silesia in Poland in the Years 2021-2022

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Introduction: Silesia is a highly industrialized region in the south of Poland. The consequences of injuries and degenerative changes are the most common diseases. The treatment uses drugs in line with WHO recommendations.

Objective: The aim of the study is to retrospectively analyze the medical records of patients treated in three analgesia clinics among patients treated with cannabinoids.

Material and methods: The material for analysis consists of the histories of diseases of 154 patients treated in 2021 and at the beginning of 2022 in three pain relief clinics located in Silesia. Patients included in the statistical analysis were treated according to the opioid, adjuvant, THC, CBD regimen at various concentrations.

Results: Women dominated among the patients (64%). Degenerative changes in the spine were the most common disease. Among patients treated with cannabinoids, 84% of patients were treated with CBD oil, most often with a concentration of 30% (68%). 43% of patients were treated with THC by vaporization (in a concentration from 18% to 22%). THC and CBD were administered most often in the evening (94% of patients).

Conclusions: During at least 3 months of treatment, an improvement in the health of patients was observed, which was expressed by a reduction of the NRS to 1-3 and an improvement in mood in 80% of patients. In 45% of patients, a reduction in the need for opioids was observed.

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Basic Science

Perception about Cannabis use: Evidence from Ghana and South Africa

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Cannabis is dangerous. It makes people mad. Cannabis is a gateway drug to other harmful substances. These popular narratives and public opinions have played a key role in influencing society's acceptance or rejection of cannabis. This study does not tackle cannabis from a moral or emotional perspective, but a purely objective and rigorous scientific perspective underpinned by the Social Information Perception (SIP) framework. The study prefaces by indicating that although there are misconceptions about cannabis, there is still a lot to unpack about its effects on human wellbeing. Drawing on a purely quantitative cross-country dataset from 1548 individuals residing in Ghana and South Africa, the study addressed the following concerns: (a) what does society know about cannabis? (b) what are the scientific claims about cannabis on human wellbeing? (c) what is the gap between perception and knowledge? Despite the little knowledge, results from the logit regression model concluded that cannabis is perceived as a harmful and dangerous substance. Irrespective of the low level of information about the plant, the study found a positive correlation between perceived use of cannabis and crime, violence, rape, and suicide. Given the above disconnect between knowledge and perception about cannabis, the study recommended the following. Firstly, knowledge enhancement and adequate advocacy. Secondly, public awareness on the pros and cons of cannabis for society to enhance understanding of the benefits and its side effects to provide evidence-based guidance on the medical application and industrial potentials.

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Basic Science

Medical cannabis Use and Self-reported Wellbeing: Evidence from South Africa

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The health benefits of medical cannabis have been debated widely at the individual, society, and global policy playgrounds. However, these arguments are anecdotal with little scientific underpinnings. Drawing on Husserl's phenomenological framework, the study explored the lived experiences of individuals using medical cannabis for wellbeing improvement. The study draws on purely qualitative data from individuals in South Africa, to provide insight on medical cannabis use and self-reported wellbeing in terms of chronic pain management, coping strategy for stress and anxiety, migraine, and cancer treatment. While some schools of thought project cannabis as a gateway drug to the infernal realm, this study provides a counter verdict based on real-time practical experience from a well-informed and educated user. Notwithstanding the immense benefits, an inappropriate, heavy, and prolonged use of high-THC strain cannabis among individuals undergoing brain development with complicated underlying health conditions and a family history of schizophrenia may harm users. In effect, the study proposes that users need to be well-informed before using medical cannabis for any health purpose.

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Basic Science

Cannabis Legalization in Ghana: Implications for Value-Addition in Medical and Industrial Research and Applications

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On 21 March 2020, Ghana's Parliament, through the Narcotics Control Commission Bill decriminalised cannabis for health and industrial purposes. The law empowers the Ministry of Interior to grant licenses for the cultivation of cannabis of not more than 0.3% tetrahydrocannabinol (THC), the active compound that gives the feeling of 'being stoned' or 'high'. Ghana joins Lesotho, Zimbabwe, Malawi, South Africa and Zambia as the few African countries that have legalised ganja. The race to legalise is strong, and unstoppable. However, knowledge in balancing the benefits and the potential downsides, as well as appropriate conditions for a successful cannabis industry is in short supply. We review the multiplicity of roles that the cannabis plant is here to play, and present a model of cannabis utilisation that simulates different supply chain paths and articulate the conditions for a successful cannabis industry. This study is exploratory, and it seeks to pose a variety of questions and puzzles for further research.

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Basic Science

Analysis of Stability Profiles for Medicinal Cannabis Inflorescence and Oil Formulations

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Background: Cannabinoid concentrations and microbiological load are amongst the parameters assessed during the regulatory review of stability profiles when establishing a shelf-life for cannabis-based products licensed in Malta. There is limited evidence in literature comparing the stability performance of different medicinal cannabis-based formulations.

Objectives: To compare the stability parameters between medicinal cannabis-based oil and flower product formulations, studied under varied storage conditions.

Methods: Data was extracted from stability studies of 13 flower and 9 oil products that are currently licensed in Malta. Results were generated under accelerated, intermediate and long-term conditions according to ICH Q1A(R2) criteria. Microbial levels and quantification values for cannabinoids were analysed, and inferential statistical tests for the mean change in cannabinoid concentration over time between flower and oil product formulations were performed.

Results: A total of 63 and 29 stability studies were reviewed for inflorescence and oil product formulations respectively. Microbiological safety levels were maintained throughout the stability period for all studies, where European Pharmacopeial microbiological standards for oral (5.1.8b) and inhalation (5.1.4) routes of administration were adhered to for flowers, with only the former limits applying to oils. The maximum deviation of the cannabinoid content from initial concentration was 11.5% for flowers and 1.25% for oils. For all 3 storage conditions, a significant difference was observed between the oil and flower formulations in terms of the rate of change in cannabinoid concentration (p0.001).

Conclusion: This study identified a statistically significant disparity in the deviation of cannabinoid concentration over time when comparing medicinal cannabis-base products in their oil and inflorescence forms.

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Basic Science

An Exploratory Review of Subjective Quality of Life Measurement in Palliative Care: A Journey over Three Decades. "Examining Quality of Life as a Dynamic Construct"

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Introduction:

Quality of life (QoL) is a very difficult outcome to measure adequately and scientifically, yet it is a vital and the most important outcome to measure in a Palliative Care population. The relationship between symptoms, their 'bother' to patients and the link to QoL as perceived by patients is analysed.

Objectives:

This exploratory review paper debates the history, philosophical aspects of QoL measurement, as an outcome measurement in health with specific attention to palliative care patients/carers and the extent to which this 'science' has evolved to place the 'patient/carer' at the core, intricately shifting and evolving with the dynamic nature of the human spirit, while maintaining scientific validation.

Methods:

A review of studies, using a subjective measure of QoL, in palliative care patients and their carers, the Schedule for the Evaluation of Quality of Life (SEIQoL) and SEIQoL-Direct-Weighting (SEIQoL-DW), were analysed.

Results:

SEIQoL, SEIQoL-DW, a modified SEIQoL-DW to assess Symptom Bother (SB), Symptom Bother Interference with QoL (SBIQoL) and measuring Response Shift (RS) were all acceptable/valid as outcome measures for Palliative Care patients and carers. When RS was incorporated, results were illuminating in the trend towards positive QoL in the face of impending mortality. Using QoL/Symptom outcome information as an actual 'Clinical Tool', in a controlled setting in an acute hospital setting, yielded very positive results.

Conclusion:

Use of QoL, SB, SBIQoL and RS information as a 'clinical tool' has been shown to improve patient's SBIQoL and could have a role in future evaluation of effective service delivery.

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Clinical Studies

A Retrospective Review of Oncology Inpatients Prescribed Sativex as an Anti-emetic and/or Appetite Stimulant in Galway University Hospital by the Palliative Medicine Service.

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Background: Manipulation of the endocannabinoid system regulates nausea and vomiting. Evidence from animal experiments suggests that cannabinoids, both delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) may be useful in treating more difficult to control symptoms of nausea, anticipatory nausea and anorexia in chemotherapy patients, which are less well controlled by the currently available conventional pharmaceutical agents. The active substances in Sativex oral spray are THC and CBD.

Objectives: To assess the effects of Sativex in Oncology inpatients with nausea, emesis and appetite.

Methods: A retrospective review of medical notes was conducted on inpatients prescribed Sativex over a 20-week period. Patient demographics, Sativex dose, duration of use and response were recorded.

Results: 34 patients were identified, data for 17 patients were excluded as either the documentation obtained was insufficient or drug not commenced. Of 17 included for analysis; 7 patients had some increase in appetite, 2 no increase; nausea, 3 complete relief, 5 partial relief; emesis, 2 complete relief, 2 partial relief and 1 no relief; 17% (n=3) no benefit.

Conclusion: Sativex has been found to be helpful in some for management of nausea, vomiting and it may produce an appetite. Use of this drug may mean less need for ‘other’ anti-emetics and the risk of extra-pyramidal side effects. Also, apart from the beneficial effect for some using pro-kinetics for anorexia, there is no other drug that effects appetite stimulation significantly. Our service is currently enrolled in a large multicenter phase 2 trial of cannabinoids for its antiemetic effects in Oncology patients.

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Basic Science

Opposite to Synthetic CBD, the High Doses of *Cannabis sativa* L. Extract Increase COX-1 and COX-2 Expression in Rats` Model of Neuropathic Pain

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Background:

The active compounds of *Cannabis sativa* L. seem to be promising in treating neuropathic pain, which remains a clinical challenge in many diseases such as: haematological, infectious, rheumatological diseases, cancers and diabetes mellitus.

Objectives:

The study aimed to assess the analgesic and anti-inflammatory effects of different doses of *Cannabis sativa* L. extract (CSLe) in treating neuropathic pain. For this, we examined the expression of cyclooxygenase 1- COX1 and cyclooxygenase 2- COX2 -enzymes involved in pain feeling and inflammatory processes.

Methods:

The rat model of neuropathic pain developed by administering vincristine was treated with gabapentin (60 mg/kg BW).

The fourteen groups of ten animals received the following concentrations of CSLe: 5,0; 7,5; 10,0; 20,0; 40,0 mg/kg BW; a separate group received 20 mg/kg BW of synthetic cannabidiol (CBD). The mRNA levels for COX-1 and COX-2 in the prefrontal cortex (PC) and hippocampus (H) were examined using q-rt-PCR.

Results:

Vincristine increased, while Gabapentin and CBD decreased the expression of COX-1 and COX-2 in PC and H (p0.005). Surprisingly, in the concentration of 10, 20, and 40 mg/kg BW CSLe exhibited the opposite of the CBD effect, increasing COX-1 and COX-2 expression in PC and H (p

Conclusions:

The synthetic CBD showed analgesic and anti-inflammatory effects in contrast to the high doses of *Cannabis sativa* L .extract. For the verification of the differences, further studies are needed.

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Clinical Studies

Tetra-hydro-cannabinol (THC), Cannabidiol (CBD) and their Combination (THC/CBD) in Peripheral Neuropathic Pain Treatment. A Randomized, Double-Blind, Placebo-Controlled Clinical Trial.

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Background: Cannabis or cannabinoids are prescribed for treatment of neuropathic pain, but the evidence is equivocal.

Objectives: To examine the effect of essential cannabinoids in peripheral neuropathic pain.

Methods: This was a randomized, double-blind, parallel group trial with treatment arms for cannabidiol (CBD), tetra-hydro-cannabinol (THC), CBD and THC combination (CBD/THC), and placebo in 1:1:1:1 ratio and flexible drug doses (CBD 5 to 50 mg, THC 2.5 mg to 25 mg, and CBD/THC 2.5 mg/5 mg to 25 mg/50 mg). Treatment period of 8 weeks duration was proceeded by 1 week for baseline observations. Patients fulfilling criteria for probable or definite neuropathic pain and failing at least one previous evidence-based treatment were eligible. The primary outcome was the change in weekly average of daily pain measured with a numeric rating scale (NRS). Trail Making Test (TMT) was used as a test of mental functioning.

Results: 145 patients were included in the study and data from 115 randomized patients were analyzed. The active treatments reduced pain, but not more than placebo ($p = 0.04 – 0.60$). Effect sizes as estimated in week 8 (positive values worse and negative better than placebo) were CBD mean 1.14 NRS points (95% CI 0.11 – 2.19), THC 0.38 (CI -0.65 – 1.4), and CBD/THC -0.12 (-1.13 – 0.89) in the ITT population. Time to perform the TMT was non-significantly increased by CBD/THC.

Conclusion: CBD, THC and their combination did not relieve peripheral neuropathic pain in patients failing at least one previous evidence-based treatment for neuropathic pain.